UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/955,373	10/21/1997	SOREN MOURITSEN	P58774US3	7254

7590 09/09/2005

Thomas J. Kowalski
FROMMER LAWRENCE & HAUG LLP
745 Fifth Avenue
New York, NY 10151

EXAMINER	
SCHWADRON, RONALD B	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 09/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/955,373	MOURITSEN ET AL.	
	Examiner	Art Unit	
	Ron Schwadron, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *56-71 and 73-84* is/are pending in the application.

4a) Of the above claim(s) *56-67,70,71 and 81-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *68,69,73-80* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Applicant's election with traverse of the species Group B and saponin in the reply filed on 10/31/2003 and 8/18/2004 is acknowledged. The traversal is on the ground(s) that are stated. This is not found persuasive because of the following reasons. Regarding applicants comments about the species election and groups A/B, said groups are distinct for the reasons elaborated in the communication mailed 7/31/2003. The searching of additional species would place a burden on the Examiner. Regarding applicants comments about the species election in paragraph 1 of the communication mailed 7/31/2003, said communication states that the species is "The method of claim 77 wherein the adjuvant is one of the agents recited in said claim.". Clearly, the aformentioned refers to the method of claim 77 and one of the agents/adjuvants recited in said claim. The searching of additional species would place a burden on the Examiner.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 55-67,70,71 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 10/31/2003 and 8/18/2004.

3. Regarding claims 80-84, applicant in the response filed 2/16/2000 had previously elected a method using TNF-α without traverse. Claims 81-84 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 2/16/2000.

4. Claims 68,69,73-80 are under consideration.

5. The information disclosure statement filed 5/23/2002 fails to comply with 37 CFR 1.97(c) because it lacks a statement as specified in 37 CFR 1.97(e) or the fee set forth in 37 CFR 1.17(p). It has been placed in the application file, but the information referred to therein has not been considered.

6. The rejection of claims 54 and 55 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the reasons elaborated in the Office action mailed 1/27/2001, paragraph 4 is withdrawn in view of the cancellation of said claims.

7. The rejection of claims 26,28,45-47,53-55 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons elaborated in the previous Office Action, paragraph 5 is withdrawn in view of the cancellation of said claims.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 68,69,73-80 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

a) There is no support in the specification as originally filed for the recitation of "ascertaining which of the different modified self-proteins elicits a desired specific neutralizing effect and thereby ascertaining a desired modified self protein" in claim 68 or 69. Regarding applicants comments, the specification, page 9 indicates that the "fine specificity of autoantibodies can be regulated, potentially enabling a tuning of the specificity towards a specificity mediating high neutralizing effect on the desired biological activity". The limitation under consideration is broader than the scope of the aformentioned limitation in the

specification (because it is not limited to potentially enabling a tuning of the specificity towards a specificity mediating high neutralizing effect on the desired biological activity). The scope of the disclosure is not commensurate with the scope of the written description provided in the specification (AKA the claimed invention constitutes new matter).

b) There is no support in the specification as originally filed for the recitation of "administering to the animal, an immunologically effective amount" in the context recited in claim 68 or 69. Said limitation is not disclosed in the specification as originally filed. The scope of the disclosure is not commensurate with the scope of the written description provided in the specification (AKA the claimed invention constitutes new matter).

c) There is no support in the specification as originally filed for the method of claims 68 or 69, lines 5-8. The specification and original claims indicate that the substitution is carried out "as to essentially preserve the overall tertiary structure of the original self-protein". While the aformentioned phrase is indefinite for the reasons elaborated in the previous Office Action, it appears to place some sort of structural limitation on the changes that are encompassed by the claimed method. The current claims encompass any substitution into the parent molecule. The scope of the disclosure is not commensurate with the scope of the written description provided in the specification (AKA the claimed invention constitutes new matter).

d) There is no support in the specification as originally filed for the method of claims 68 or 69 because the invention as disclosed in the specification is limited to the use of recombinantly produced modified self proteins whilst claims 68 and 69 are not. The scope of the disclosure is not commensurate with the scope of the written description provided in the specification (AKA the claimed invention constitutes new matter).

10. The rejection of claims 26,28,45,46,54,55 under 35 U.S.C. 102(b) as being anticipated by Russell-Jones et al. (WO 92/05192) for the reasons elaborated in the previous Office Action is withdrawn in view of the cancellation of said claims.

11. The rejection of claims 26,28,45-47,53-55 under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. (WO 92/05192) in view of Hellman (WO 93/05810), Etlinger and prior art disclosed in the specification (page 18, last paragraph) is withdrawn in view of the cancellation of said claims.

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 68,69,73,76,77,78 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. in view of Zanetti et al. (US Patent 5,658,762), Wolfson et al., Lowenadler et al. and prior art disclosed in the specification (page 2, Talwar et al.)

Russell-Jones et al. teach T cell epitopes derived from Trat protein (see Abstract). Russell-Jones et al. teach Trat T cell epitopes are inserted into proteins, wherein the insertion of said peptide increases the antibody response against the protein into which Trat has been inserted (see page 4, lines 24-26, page 31, lines 4-8, claim 14 and Abstract). Russell-Jones et al. teach that the Trat peptide is inserted such that the protein still functions as an immunogen.

Russell-Jones et al. teach that the Trat modified immunogen can be used as a vaccine in a composition containing an adjuvant such as saponin (see page 8 and 13). Russell-Jones et al. teach that using recombinant DNA technology that Trat peptide can be inserted into the immunogen via substituting Trat peptide for a peptide contained in said molecule (see page 31, first incomplete paragraph and claim 14 wherein the nucleic acid of claim 14 is used to recombinantly produce said protein). Russell-Jones et al. teach that immunogens used in the aforementioned vaccines can include self proteins such as luteinizing hormone, somatostatin, inhibin, FSH (see page 9 and claim 12). The production of antibodies against a self protein would constitute "breaking B cell autotolerance". Russell-Jones et al. teach that such vaccines can be used in animals and humans. While the immunogens disclosed by Russell-Jones et al. would encompass the human protein, the use of human fertility related proteins in vivo(such as human hCG) was known in the art (see Talwar et al. as per disclosed in the specification as prior art). Russell-Jones et al. teach that different Trat peptides are screened to establish which peptides have the greatest efficacy (see Example 4). Russell-Jones et al. do not specifically teach that the method includes screening of different positions of the inserted epitope to determine the desired neutralizing effect. It would be routine optimization to determine which position of the inserted epitope elicits the best desired neutralizing effect. Furthermore Russell-Jones et al. disclose that it is desireable to optimize the hybrid immunogen used (see page 9, last paragraph, continued on next page). Additionally, Lowenadler et al. disclose addition of a T cell epitope into a protein, wherein the position of insertion is optimized to determine the most efficacious site of placement (see pages 1186-1187). The substitution of functionally active peptides into a foreign protein was well known in the art (for example see Zanetti et al. or Wolfson et al. or Lowenadler et al.). Zanetti et al. teach that a epitope was added to a protein wherein the added epitope was 15 amino acids in length (see column 11, first complete paragraph). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Russell-Jones et al. teach Trat T cell epitopes are inserted into proteins, wherein the insertion of said peptide

increases the antibody response against the protein into which Trat has been inserted and that immunogens used in the aforementioned vaccines can include self proteins and it would be routine optimization to determine which position of the inserted epitope elicits the best desired neutralizing effect, Lowenadler et al. disclose addition of a T cell epitope into a protein, wherein the position of insertion is optimized to determine the most efficacious site of placement and the substitution of functionally active peptides into a foreign protein was well known in the art. One of ordinary skill in the art would have been motivated to do the aformentioned because Russell-Jones et al. teach that immunogens used in the aforementioned vaccines can include self proteins and Russell-Jones et al. and Lowenadler et al. disclose that it is desireable to optimize the hybrid immunogen used.

Regarding applicants comments in the amendment filed 5/23/2002, the claims were subsequently amended in the amendments filed 12/9/2002 and 3/24/2003 such that the amendment filed 5/23/2002 largely addresses limitations no longer found in the claims as per the amendments of 12/9/2002 and 3/24/2003. Regarding the issue of "suppressor regions", and the various Travers and Zinkernagel declarations, Example 5 is simply one example in the Russell-Jones et al. publication. Russell-Jones et al. teach Trat T cell epitopes are inserted into proteins, wherein the insertion of said peptide increases the antibody response against the protein into which Trat has been inserted (see page 4, lines 24-26, page 31, lines 4-8, claim 14 and Abstract). Russell-Jones et al. teach that the Trat peptide is inserted such that the protein still functions as an immunogen. Russell-Jones et al. teach that the Trat modified immunogen can be used as a vaccine in a composition containing an adjuvant such as saponin (see page 8 and 13). Russell-Jones et al. teach that using recombinant DNA technology that Trat peptide can be inserted into the immunogen via substituting Trat peptide for a peptide contained in said molecule (see page 31, first incomplete paragraph and claim 14 wherein the nucleic acid of claim 14 is used to recombinantly produce said protein). Russell-Jones et al. teach that immunogens used in the aforementioned vaccines can include self proteins such as luteinizing hormone, somatostatin, inhibin, FSH (see page 9 and claim 12).

Russell-Jones et al. teach that such vaccines can be used in animals and humans. Assuming arguendo that Example 5 was not present, Russell-Jones et al. still teaches the aforementioned aspects of the clamed invention. Regarding the use of human proteins, Russell-Jones et al. teach that immunogens used in the aforementioned vaccines can include self proteins such as luteinizing hormone, somatostatin, inhibin, FSH (see page 9 and claim 12). Russell-Jones et al. teach that such vaccines can be used in animals and humans. While the immunogens disclosed by Russell-Jones et al. would encompass the human protein, the use of human fertility related proteins in vivo(such as human hCG) was known in the art (see Talwar et al. as per disclosed in the specification as prior art). Regarding the Schmidt and Borregaard declarations and the issue of commercial success, there is no evidence of record in either declaration that a product was actually produced and sold. In fact, said declarations establish that many years after the filing date of the instant application that applicants are still attempting to establish whether their method can even be used to treat disease. Furthermore, it also unclear as what "AutoVac technology" encompasses and the relationship of "AutoVac technology" to the disclosure of the claimed invention is also unclear. It is also noted that the filed IDS was not considered and the references listed on said IDS were not considered. It is also noted that the various declarations were of record as of the interview of 11/14/2002 wherein the pending rejections at that time were maintained.

14. Claims 74,75,79,80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Russell-Jones et al. in view of Zanetti et al. (US Patent 5,658,762), Lowenadler et al., Wolfson et al. and prior art disclosed in the specification (page 2, Talwar et al.) as applied to claims 68,69,73,76,77,78 above, and further in view of Hellman (WO 93/05810) and Le et al. (US Patent 5,698,195).

The previous rejection renders obvious the claimed invention except for use of TNFα. Hellman teaches that modulation of self proteins responsible for manifestations of a particular disease can be achieved using self-protein conjugated to a carrier which is recognized by T helper cells(see pages 5-12) and wherein the administered hybrid molecule elicits antibodies against said

molecule. Le et al. teach that antibodies against TNFα are used to treat TNFα mediated diseases in humans (see abstract and column 5). It would have been prima facies obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the use of anti TNFα antibodies to treat TNFα mediated disease was known in the art, Hellman teaches that modulation of self proteins responsible for manifestations of a particular disease can be achieved by inducing antibodies against said molecules using self molecules that contain T helper epitopes and Russell-Jones et al. teach methods for inducing antibodies against self proteins using Trat modified molecules.

15. No claim is allowed.

16. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ron Schwadron, Ph.D. whose telephone number is 571 272-0851. The examiner can normally be reached on Monday-Thursday 7:30-6:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571 272-0841. The fax phone number for the organization where this application or

proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

..ONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644